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Review article

Epidemiology of Human Papillomavirus (HPV) Infection among Iranian Women Identified with Cervical Infections: A Systematic Review and Meta-Analysis of National Data

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Abstract

Background: Human papillomavirus (HPV) is one of the most common causes of sexually transmitted disease (STD) in humans. HPV is associated with gynecologic malignancy and cervical cancer among women worldwide. In the current study we sought to determine the prevalence rate of HPV in Iranian women identified with cervical infections.
Materials and Methods: Prevalence rate of HPV in Iran was investigated from 2000-2016 using several databases including Medline, Web of Science, Embase, Google Scholar, Iranmedex, and Scientific Information Database. Statistical analysis was performed by Comprehensive Meta-Analysis (V2.2, Biostat) software. Random effects models were used by taking into account the possibility of the heterogeneity between the studies, which was tested through the Cochran's Q-statistic.
Results: The meta-analyses showed that the prevalence rate of HPV infections was 38.6 % (95% CI, 27.9-50.5) among Iranian women with cervical infections. The further stratified analyses indicated that the prevalence rate of HPV was higher in the studies conducted during the 2000-2008 years.
Conclusion: The results of the present study underscore the need for further enforcement of STD control strategies in Iran. Establishing advanced diagnostic facilities for HPV, vaccination of high risk groups, and continuous monitoring of HPV are recommended for HPV prevention and control.

Key words: Human papillomavirus, HPV, Cervical infection, Iran, Meta-analysis

1. Background

Human Papillomavirus (HPV) was initially recognized in patients with cervical cancer and is one of the most important sexually transmitted viruses in the world (1-3). There are more than 100 known HPV types, of which more than 10 types have been associated with genital cancer (4). Infections caused by carcinogenic HPV types are considered as the major reasons for increase in all cervix infections, invasive cervical region cancer, and neoplasia of intraepithelial cervical carcinoma (5-7). Cervical cancer is one of the usual abnormalities in females' cervix (8), which is the third most common lethal cancer in women with an estimation of 530,000 reports and 275,000 mortality rate in the world per year (9). Investigations conducted in several countries to evaluated the HPV-DNA, indicated that 6.6% of the patients with the age ranges from 15 to74 years were HPV-DNA positive (10). Thus, HPV can be regarded as one of the most important agents causing sexually transmitted diseases (STD) in the world. HPV infections have been indicated to be associated with increased risk of cervix carcinoma (11-12). According to the studies, HPV is responsible for more than 5% of the entire carcinoma worldwide (4, 13-14). In addition, other microorganisms such as *Mycoplasma genitalium*, *Chlamydia trachomatis,* and *Neisseria gonorrhea* are also known as risk factors for the genital area cancers (15-17). Till date, there are limited studies on HPV prevalence in different areas of Iran.

2. Objective

The current study was aimed to investigate the true prevalence rate of HPV among Iranian women identified with cervical infections using a systematic review and meta-analysis according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.

3. Materials and Methods

3.1. Literature Search

A database was built for the prevalence rate of HPV in Iran from 2000 to 2016 using several databases including Medline (via PubMed), Web of Science, Embase, Google Scholar, Iran medex, and Scientific Information Database (SID). The research was restricted to the original articles published in English and Persian, presenting the prevalence or incidence of HPV in health-care settings in Iran. The following keywords were used from medical subject headings, titles, or abstracts with the help of Boolean operators (and, or): Human Papilloma Virus, HPV, Prevalence, Cervix, Cervical Cancer, Incidence, and Iran. We also searched bibliographies of retrieved articles for additional references. In addition to articles published in English, we also looked for relevant articles in Persian.

3.2. Inclusion and exclusion criteria

All original articles presenting cross-sectional studies on the prevalence rate of HPV in Iran were reviewed. The selection of the articles to be reviewed was done in three

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stages: titles, abstracts, and full texts. Included studies had the following criteria: using standard methods for HPV molecular testing and presenting data on the number of enrolled patients. For safety evaluation, we further included studies conducted on more than 100 subjects. Review articles, studies reported in languages other than English or Persian, meta-analyses or systematic reviews, duplicated publication of the same study, and articles available only in abstract form were excluded from our study. To minimize the potential bias caused by too small sample size, studies with less than 50 subjects were excluded.

3.3. Data extraction

The following variables were extracted from the included studies: author's name, study time, publication year, settings, the number of investigated patients, and the number of HPV isolates, and the source of isolates. Prevalence of HPV was extracted as well. Two investigator extracted data from all of the included studies independently. Inconsistencies between the reviewers were discussed in order to obtain consensus.

3.4. Quality assessment

Included studies were appraised for quality using a quality assessment checklist, which was designed by Joanna Briggs Institute.

3.5. Meta-Analysis

Analysis was performed using Comprehensive Meta-Analysis (V2.2, Bio stat) software. Generally, we used fixed or random effects models depending on the statistical heterogeneity between the studies to calculate summary estimates. Statistical heterogeneity was quantified by I_2 statistic. In order to assess possible publication bias, Egger weighted regression methods were used. Value of $P < .05$ was considered as an indicative of statistically significant publication bias.

4. Results

4.1. Characteristics of Included Studies

Initially, a total of 55 articles were collected. In secondary screening, 24 cases were excluded based on the title and abstract evaluation (Figure 1). In the next step, 9 out of 31 remaining studies were excluded based on the full text search. At the end, 22 eligible studies were chosen for final analysis. Figure 1 shows why records were excluded based on the assessment of title, abstract, and articles full text.

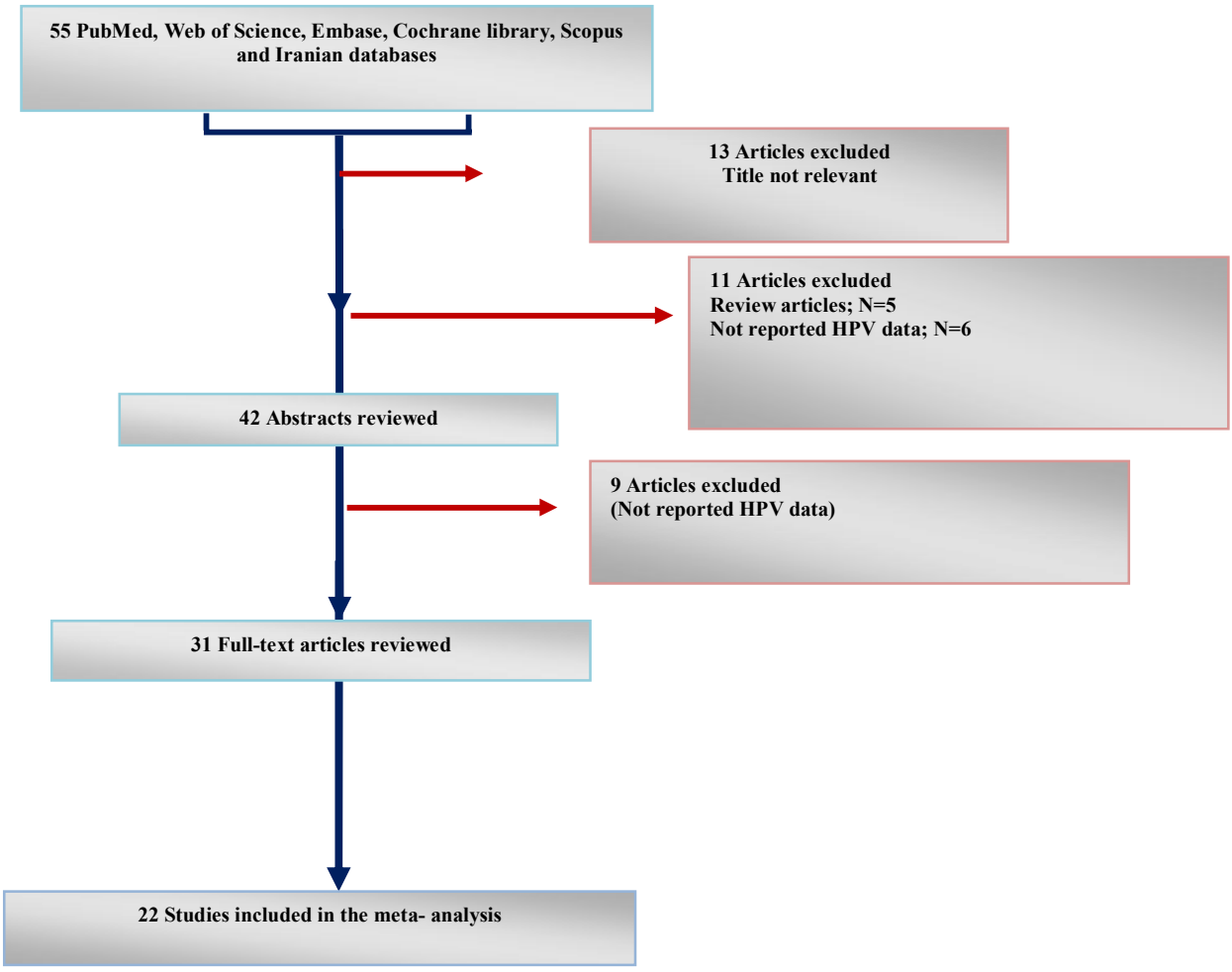

Figure 1. Flow diagram of literature search and study selection.

4.2. The Prevalence of HPV

The pooled prevalence rate of HPV infections among molecular testing-positive cases of HPV was 38.6 (95% CI, 27.9-50.5) (Table 1). The heterogeneity test indicated that there were heterogeneities between the studies (I_2 = 94.786, P < .001). The forest plot of HPV prevalence meta-analysis is shown in Figure 2. As shown in Table 1 and Figure 3, no evidence of publication bias was observed (P > .05 for Egger weighted regression analysis).

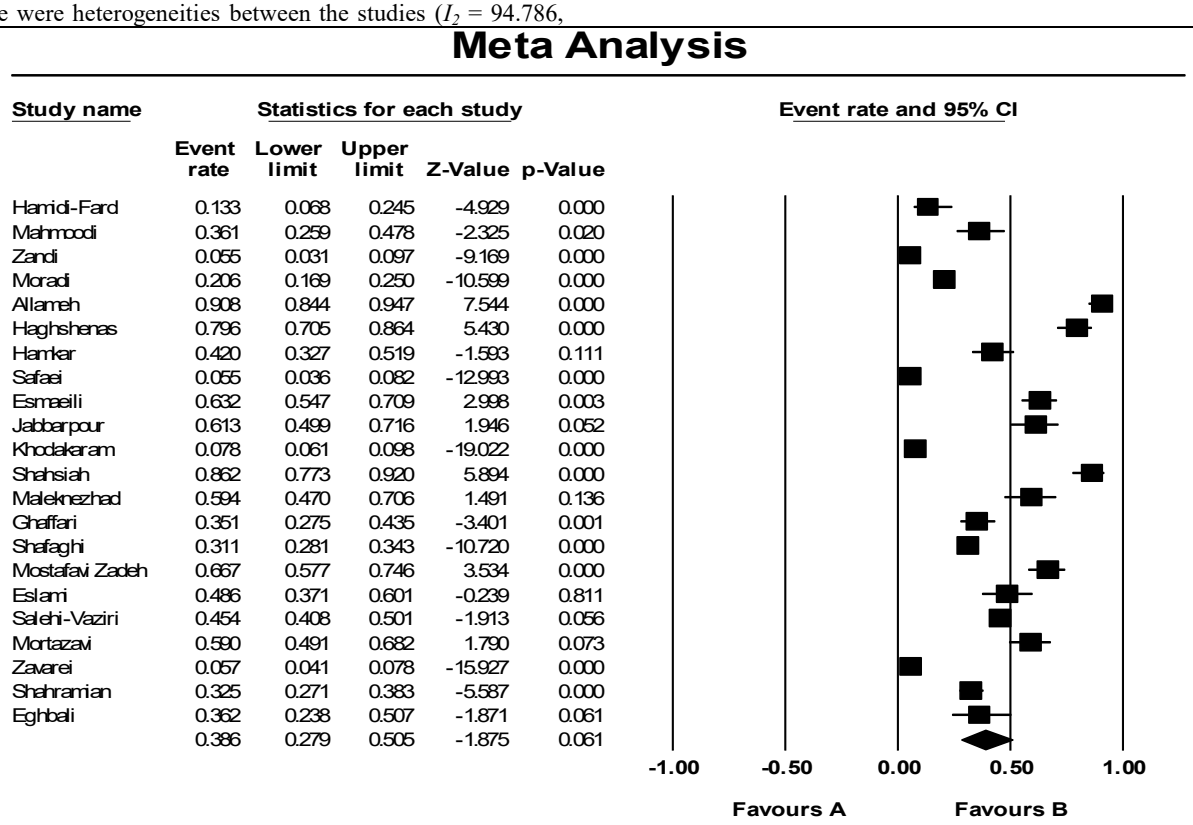

Figure 2. Forest plot of the meta-analysis on prevalence of HPV in cervical samples of Iranian patients.

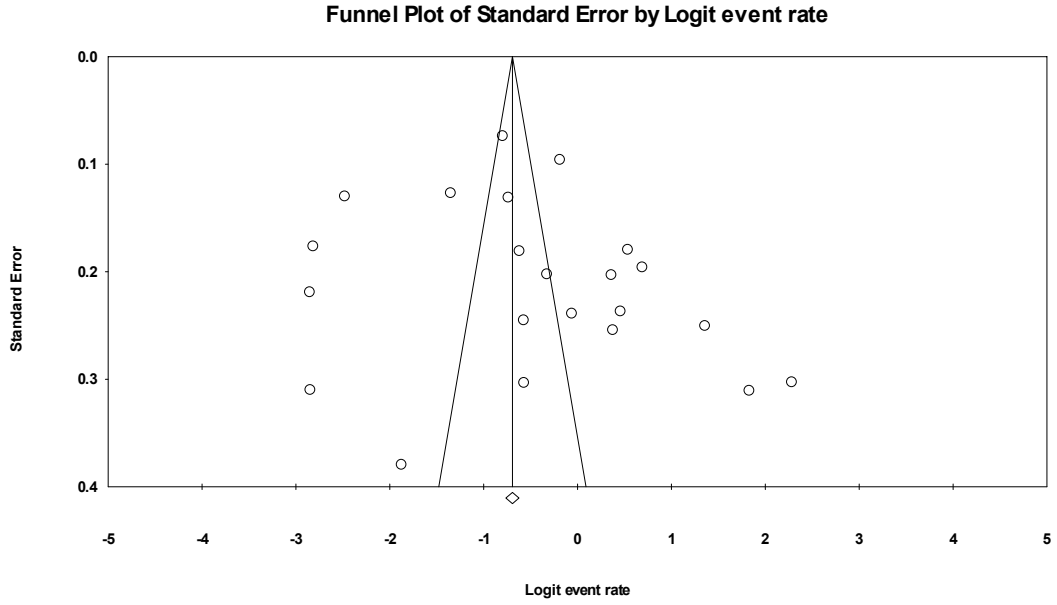

Figure 3. Funnel plot of the meta-analysis on prevalence of HPV in cervical samples of Iranian patients.

Table 1. Meta-analysis of prevalence of HPV infections in cervical samples of Iranian patients.

Subgroups	No. of study	Prevalence of HPV (95% CI)	n/N	Heterogeneity test, I2 (%)	Heterogeneity test, *P* value	Egger's test, t	Egger's test, *P* value
Overall effects	22	38.6(27.9-50.5)	1508/5244	94.786	<.001	0.983	.336
Research period 2000-2008 (30-41)	12	46.5(28.2-65.8)	685/2160	94.861	<.001	1.700	.119
Research period 2009-2016 (42-51)	10	29.9(18.3-44.9)	823/3084	94.805	<.001	0.037	.971

n = Number of HPV / N = Number of cervical samples

5. Discussion

The present systematic review and meta-analysis indicated the prevalence rate of HPV infections in Iranian patients identified with cervical infections. Our analyses showed that the prevalence rate of HPV infections was 38.6% (95% CI, 27.9-50.5) among Iranian women with cervical infections (Table 1). Such a high prevalence rate of HPV (38.6%) among women with cervical infections may be due to several factors (18-19). First, lack of hygiene and organized screening programs for prevention and control of STD. The second factor which can be accounted for the high prevalence rate of HPV is the insufficient information available about some types of HPV responsible for infections (20). It seems that the determination of HPV types is very important for designing programs suitable for infection control and treatment (21-23).

Our results also showed an increase in HPV prevalence rate (46.5%) during the 2000-2008 years (95% CI, 28.2-65.8) in comparison with the studies conducted during the 2009-2016 years (Table 1). Observed decrease in HPV prevalence rate in recent years could be due to such reasons as: the use of HPV vaccine and the increased hygiene level in different Iranian populations (24-25). Previous studies reported different HPV prevalence ranges in cervical infections, even some studies were unable to report HPV in cervical infections (26-29). The different results in the studies conducted in Iran could be attributed to such factors as the studies condition; the type of histopathological sampling; sample transferring and storage condition; the type of method used for HPV detection; molecular technique; time of study; and patient's age, racial and ethnicity.

There are some limitations for this study that should be discussed. First of all, only published studies were accepted to be included in the present meta-analysis. Thus, as with any systematic review, the existence of the potential publication bias should be accounted for. Second, heterogeneity was detected among the included studies. Third, it wasn't able to fully represent the prevalence rate of HPV in Iran because the extent of HPV has not yet been examined in some regions of Iran.

6. Conclusions

The results of the present study underscore the need for further enforcement of STD control strategies in Iran. Establishing advanced diagnostic facilities for HPV, vaccination of high risk groups, and continuous monitoring of HPV are recommended for HPV prevention and control.

Conflict of interest

We declare that we have no conflict of interest.

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Authors' Contribution

All of authors contribute to this study.

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References

1. Vinodhini K, Shanmughapriya S, Das BC, Natarajaseenivasan K. Prevalence and risk factors of HPV infection among women from various provinces of the world. Arch Gynecol Obstet. 2012; 285(3):771-7.
2. Liu X, Zhang S, Ruan Q, Ji Y, Ma L, Zhang Y. Prevalence and type distribution of human papillomavirus in women with cervical lesions in Liaoning Province, China. Int J Gynecol Cancer. 2010; 20(1):147-53.
3. Steben M, Duarte-Franco E. Human papillomavirus infection: epidemiology and pathophysiology. Gynecol Oncol. 2007; 107(2 Suppl 1):S2-5.
4. De Sanjosé S, Diaz M, Castellsagué X, Clifford G, Bruni L, Muñoz N, et al. Worldwide prevalence and genotype distribution of cervical human papillomavirus DNA in women with normal cytology: a meta-analysis. Lancet Infect Dis. 2007; 7(7):453-9.
5. Chen W, Zhang X, Molijn A, Jenkins D, Shi J-F, Quint W, et al. Human papillomavirus type-distribution in cervical cancer in China: the importance of HPV 16 and 18. Cancer Causes Control. 2009; 20(9):1705-13.
6. Munoz N, Bosch F, De Sanjosé S, Vergara A, Del Moral A, Munoz M, et al. Risk factors for cervical intraepithelial neoplasia grade III/carcinoma in situ in Spain and Colombia. Cancer Epidemiol Biomarkers Prev. 1993; 2(5):423-31.
7. Muñoz N, Bosch FX, de Sanjosé S, Herrero R, Castellsagué X, Shah KV, et al. Epidemiologic classification of human papillomavirus types associated with cervical cancer. N Engl J Med. 2003; 348(6):518-27.
8. Paul MP, Iannuzzi MC. Sarcoidosis and immunoligic lung. 2011.
9. Zhao FH, Lewkowitz AK, Hu SY, Chen F, Li LY, Zhang QM, et al. Prevalence of human papillomavirus and cervical intraepithelial neoplasia in China: A pooled analysis of 17 population-based studies. Int J cancer. 2012; 131(12):2929-38.
10. Clifford G, Gallus S, Herrero R, Munoz N, Snijders P, Vaccarella S, et al. Worldwide distribution of human papillomavirus types in cytologically normal women in the International Agency for Research on Cancer HPV prevalence surveys: a pooled analysis. Lancet. 2005; 366(9490):991-8.
11. Peto J, Gilham C, Deacon J, Taylor C, Evans C, Binns W, et al. Cervical HPV infection and neoplasia in a large population-based prospective study: the Manchester cohort. Br J Cancer. 2004; 91(5):942-53.
12. Maucort-Boulch D, Franceschi S, Plummer M. International correlation between human papillomavirus prevalence and cervical cancer incidence. Cancer Epidemiol Biomarkers Prev. 2008; 17(3):717-20.
13. Radojicic J, Zaravinos A, Spandidos DA, Agostini M, Bedin C, Pucciarelli S, et al. HPV, KRAS mutations, alcohol consumption and tobacco smoking effects on esophageal squamous-cell carcinoma carcinogenesis. Int J Biol Markers. 2012; 27(1):1-12.

14. Parkin DM, Monteleone P, Maj M, Fusco M, Orazzo C, Kemali D, et al. The global health burden of infection-associated cancers in the year 2002. J Prev Med Public Health. 2001; 34(4):372-8.
15. Nakashima K, Shigehara K, Kawaguchi S, Wakatsuki A, Kobori Y, Nakashima K, et al. Prevalence of human papillomavirus infection in the oropharynx and urine among sexually active men: a comparative study of infection by papillomavirus and other organisms, including Neisseria gonorrhoeae, Chlamydia trachomatis, Mycoplasma spp., and Ureaplasma spp. BMC Infect Dis. 2014; 14(1):43.
16. Park H, Sim S-m, Lee G. The presence of Chlamydia is associated with increased leukocyte counts and pain severity in men with chronic pelvic pain syndrome. Urology. 2015; 85(3):574-9.
17. Dadashi M, Eslami G, Ghalavand Z, Goudarzi H, Fallah F, Owlia P, et al. Prevalence of chlamydia trachomatis and mycoplasma genitalium in patients with benign and malignant ovarian cancer by nested PCR method. Novel Biomed. 2016; 4(1):18-23.
18. Sankaranarayanan R, Qiao Y-l, Keita N. The next steps in cervical screening. Women Health. 2015; 11(2):201-12.
19. León-Maldonado L, Wentzell E, Brown B, Allen-Leigh B, Torres-Ibarra L, Salmerón J, et al. Perceptions and experiences of human papillomavirus (HPV) infection and testing among low-income Mexican women. PloS One. 2016; 11(5):e0153367.
20. Joura EA, Giuliano AR, Iversen O-E, Bouchard C, Mao C, Mehlsen J, et al. A 9-valent HPV vaccine against infection and intraepithelial neoplasia in women. N Engl J Med. 2015; 372(8):711-23.
21. Printz C. FDA approves Gardasil 9 for more types of HPV. Cancer. 2015;121(8):1156-7.
22. Bzhalava D, Eklund C, Dillner J. International standardization and classification of human papillomavirus types. Virology. 2015;476:341-4.
23. Tjalma WA. There are two prophylactic human papillomavirus vaccines against cancer, and they are different. J Clin Oncol. 2015: 33(8):964-65.
24. Delany-Moretlwe S, Cowan FM, Busza J, Bolton-Moore C, Kelley K, Fairlie L. Providing comprehensive health services for young key populations: needs, barriers and gaps. HIV and adolescents: focus on young key populations. J Int AIDS Soc. 2015:8(2 suppl1);19833.
25. Owsianka B, Gańczak M. Evaluation of human papilloma virus (HPV) vaccination strategies and vaccination coverage in adolescent girls worldwide. Przegl Epidemiol. 2015; 69(1):53-8.
26. Anttila M, Syrjänen S, Ji H, Saarikoski S, Syrjänen K. Failure to demonstrate human papillomavirus DNA in epithelial ovarian cancer by general primer PCR. Gynecol Oncol. 1999;72(3):337-41.
27. Atalay F, Taskiran C, Taner MZ, Pak I, Or M, Tuncer S. Detection of human papillomavirus DNA and genotyping in patients with epithelial ovarian carcinoma. J Obstet Gynaecol Res. 2007; 33(6):823-8.
28. Idahl A, Lundin E, Elgh F, Jurstrand M, Møller JK, Marklund I, et al. Chlamydia trachomatis, Mycoplasma genitalium, Neisseria gonorrhoeae, human papillomavirus, and polyomavirus are not detectable in human tissue with epithelial ovarian cancer, borderline tumor, or benign conditions. Am J Obstet Gynecol. 2010; 202(1):71. e1-. e6.
29. Rosa MI, Silva GD, de Azedo Simões PWT, Souza MV, Panatto APR, Simon CS, et al. The prevalence of human papillomavirus in ovarian cancer: a systematic review. Int J Gynecol Cancer. 2013; 23(3):437-41.
30. Allameh T, Moghim S, Asadi-Zeidabadi M. A survey on the prevalence of high-risk subtypes of human papilloma virus among women with cervical neoplasia in Isfahan University of Medical Science. Arch Gynecol Obstet. 2011; 284(6):1509-13.
31. Eslami G, Golshani M, Rakhshan M, Fallah F, Goudarzi H, Taghavi A. PCR detection and high risk typing of human papillomavirus DNA in cervical cancer in Iranian women. Cancer Ther. 2008;6:361-6.
32. Esmaeili M, Bonyadi M, Dastranj A, Alizadeh M, Melli MS, Shobeiri MJ. HPV typing in women with cervical precancerous and cancerous lesions in northwestern Iran. Gynecol obstet invest. 2008;66(1):68-72.
33. Ghaffari SR, Sabokbar T, Mollahajian H, Dastan J, Ramezanzadeh F, Ensani F, et al. Prevalence of human papillomavirus genotypes in women with normal and abnormal cervical cytology in Iran. Asian Pac J Cancer Prev. 2006;7(4):529-32.
34. Hamkar R, Azad TM, Mahmoodi M, Seyedirashti S, Severini A, Nategh R. Prevalence of human papillomavirus in Mazandaran province, Islamic Republic of Iran. East Mediterr Health J. 2002; 8(6):805-11.
35. Esmaeili M, Bonyadi M, Dastranj A, Alizadeh M, Melli M, S, Shobeiri M, J, HPV Typing in Women with Cervical Precancerous and Cancerous Lesions in Northwestern Iran. Gynecol Obstet Invest 2008;66:68-72
36. Maleknejad P, Rakhshan M, Kazemi B, Farokh F, Shahsava S. Detection of human papilomavirus types 16 and 18 in pathologic samples from patients with cervical cancer by PCR and RFLP methods. DARU J Pharm Sci. 2006; 14(2):78-81.
37. Mortazavi S, Zali M, Raoufi M, Nadji M, Kowsarian P, Nowroozi A. The prevalence of human papillomavirus in cervical cancer in Iran. Asian Pac J Cancer Prev. 2002;3(1):69-72.
38. Safaei A, Khanlari M, Momtahen M, Monabati A, Robati M, Amooei S, et al. Prevalence of high-risk human papillomavirus types 16 and 18 in healthy women with cytologically negative pap smear in Iran. Indian J Pathol Microbiol. 2010; 53(4):681.
39. Shahramian I, Heidari Z, Mahmoudzadeh-Sagheb H, Moradi A, Forghani F. Prevalence of HPV Infection and high risk HPV genotypes (16, 18), among monogamous and polygamous women, In Zabol, Iran. Iran J Public Health. 2011; 40(3):113-121.
40. Shahsiah R, Khademalhosseini M, Mehrdad N, Ramezani F, Nadji SA. Human papillomavirus genotypes in Iranian patients with cervical cancer. Pathol Res Pract. 2011; 207(12):754-7.
41. Zavarei MJZJ, Hamkar R, Dana VG, Delforoosh M, Shojamoradi M, Gilani MM. Prevalence of HPV infection and its association with cytological abnormalities of Pap smears in Tehran. Iran J Public Health. 2008; 37(3):101-6.
42. Eghbali M, Sadeghi F, Mirinargesi M, Mohseni R. Frequency of human papillomavirus among pregnant women by PCR technique. Int J Mol Clin Microbiol. 2013; 2:285-8.
43. Haghshenas M, Golini-Moghaddam T, Rafiei A, Emadeian O, Shykhpour A, Ashrafi GH. Prevalence and type distribution of high-risk human papillomavirus in patients with cervical cancer: a population-based study. Infect Agent Cancer. 2013; 8(1):20.
44. Hamidi-Fard M, Fattahi-Abdizadeh M, Makvandi M, Ranjbari N, Mansoori E, Samarbaf-Zadeh A. Detection and genotyping of human papillomavirus in cervical tissue samples in Ahvaz, Southwest Iran. Jundishapur J Microbiol. 2013;6(7): e4569.
45. Khodakarami N, Clifford GM, Yavari P, Farzaneh F, Salehpour S, Broutet N, et al. Human papillomavirus infection in women with and without cervical cancer in Tehran, Iran. Int J Cancer. 2012; 131(2):E156-61.
46. Mahmoodi P, Motamedi H, Shapouri MRSA, Shehni MB, Kargar M. Molecular detection and typing of human papillomaviruses in paraffin-embedded cervical cancer and pre-cancer tissue specimens. Iran J Cancer Prev. 2016;9(1): e3752.
47. Moradi A, Nosrat SB, Besharat S. Molecular epidemiology of high-risk types of human papillomaviruses (16, 18) in pap-smear, the North East of Iran. Iran J Cancer Prev. 2011;4(3):135-40.
48. Salehi-Vaziri M, Sadeghi F, Hashemi FS, Haeri H, Bokharaei-Salim F, Monavari SH, et al. Distribution of human papillomavirus genotypes in Iranian women according to the severity of the cervical Llsion. Iran Red Crescent Med J. 2016; 18(4): e24458.
49. Shafaghi B, Jarollahi A, Yousefzadeh B, Ameri A, Moghadam S, Mostafavi M. Human papilloma virus prevalence and types among Iranian women attending regular gynecological visits. Rep Radiother Oncol. 2013;1(2).
50. Piroozmand A, Mostafavi Zadeh SM, Niakan M, Madani A, Soleimani R, Nedaeinia R, et al. The association of high risk human papillomaviruses in patients with cervical cancer: an evidence based study on patients with squamous cell dysplasia or carcinoma for evaluation of 23 human papilloma virus genotypes. Cervical Cancer. 2016; 17; 9(4):e32728..
51. Zandi K, Eghbali SS, Hamkar R, Ahmadi S, Deilami I, Nejad HA, et al. Prevalence of various human papillomavirus (HPV) genotypes among women who subjected to routine pap smear test in Bushehr city (South west of Iran) 2008-2009. Virol J. 2010;7(1):65.

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